FORM PTO-1390 (REV 10-95) | U.S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTORNEY'S DOCKET NUMBER: MERCK 2337

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. §371

U.S. APPLICATION NO. (If known, see 37 CFR §1 5): 10/009614

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/05204	6 JUNE 2000	16 JUNE 1999

TITLE OF INVENTION: DEVICE FOR INTRODUCING SAMPLES

APPLICANT(S) FOR DO/EO/US: EISENBEISS, Friedhelm, et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ■ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. §371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. §371.
3. ☐ This express request to begin national examination procedures (35 U.S.C. §371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. §371(b) and PCT Articles 22 and 39(1).
4. ■ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ■ A copy of the International Application as filed (35 U.S.C. §371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ■ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ■ A translation of the International Application into English (35 U.S.C. §371(c)(2)).
7. ■ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ■ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. §371(c)(3)).
9. ■ An oath or declaration of the inventor(s) (35 U.S.C. §371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 C.F.R. §§1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. §§3.28 and 3.31 is included.
13. ■ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☐ Other items or information:

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/009614	PCT/EP00/05204	MERCK 2337

17. ☒ The following fees are submitted:

	CALCULATIONS (PTO USE ONLY)
BASIC NATIONAL FEE (37 CFR §1.492 (a) (1) - (5)):	
Search Report has been prepared by the EPO or JPO..... $890.00	
International preliminary examination fee paid to USPTO (37 CFR §1.482)..... $710.00	
No international preliminary examination fee paid to USPTO (37 CFR §1.482) but international search fee paid to USPTO (37 CFR §1.445(a)(2))..... $740.00	
Neither international preliminary examination fee (37 CFR §1.482) nor international search fee (37 CFR §1.445(a)(2)) paid to USPTO..... $1040.00	
International preliminary examination fee paid to USPTO (37 CFR §1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)..... $100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$890.00
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. §1.492(e)).	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	6 - 20 =	0	x $ 18.00	$0.00
Independent claims	1 - 3 =	0	x $ 84.00	$0.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $ 280.00	
TOTAL OF ABOVE CALCULATIONS =				$890.00
Reduction of 1/2 for filing by small entity, if applicable. A Verified Small Entity Statement must also be				
SUBTOTAL =				$890.00
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. §1.492(f)).				
TOTAL NATIONAL FEE =				$890.00
Fee for recording the enclosed assignment (37 C.F.R. §1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. §§3.28, 3.31). $40.00 per property.				
TOTAL FEES ENCLOSED =				$890.00
			Amount to be refunded:	
			charged:	

a. ■ A check in the amount of $890.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 13-3402 in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

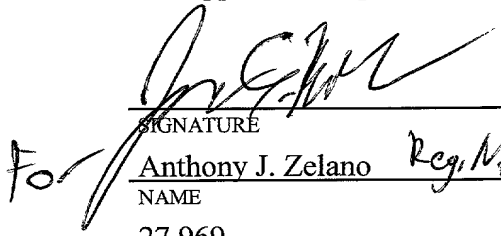
c. ■ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 13-3402. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 C.F.R. §§1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. §1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO: Customer Number 23,599

23599
PATENT TRADEMARK OFFICE

Filed: 14 DECEMBER 2001
AJZ:kmo



SIGNATURE
For Anthony J. Zelano Reg. No. 37,732
NAME
27,969
REGISTRATION NUMBER

IN THE UNITED STATES DESIGNATED/ELECTED OFFICE

International Application No.	:	PCT/EP00/05204
International Filing Date	:	6 JUNE 2000
Priority Date(s) Claimed	:	16 JUNE 1999
Applicant(s) (DO/EO/US)	:	EISENBEISS, Friedhelm, et al.

Title: DEVICE FOR INTRODUCING SAMPLES

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

SIR:

Prior to calculating the national fee, and prior to examination in the National Phase of the above-identified International application, please amend as follows:

IN THE CLAIMS:

3. (Amended) Apparatus according to Claim 1, characterized in that the channel system contains at least two serial channel sections, each of which is delimited by fluidic connections.

4. (Amended) Apparatus according to Claim 1, characterized in that the channel system contains at least two parallel channel sections which are delimited independently of one another by fluidic connections.

5. (Amended) Apparatus according to Claim 1, characterized in that tightly sealing micropumps serve as fluidic connections.

6. (Amended) Apparatus according to Claim 1, characterized in that micromixers, valves and micropumps serve as fluidic connections.

REMARKS

The purpose of this Preliminary Amendment is to eliminate multiple dependent claims in order to avoid the additional fee. Applicants reserve the right to reintroduce claims to canceled combined subject matter.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned **"Version With Markings to Show Changes Made"**.

Respectfully submitted,

For Reg. No. 37,432

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AJZ:jmm

VERSION WITH MARKINGS TO SHOW CHANGES MADE:

Claims 3 - 6 have been amended as follows:

3. (Amended) Apparatus according to Claim 1 ~~or 2~~, characterized in that the channel system contains at least two serial channel sections, each of which is delimited by fluidic connections.

4. (Amended) Apparatus according to ~~one of~~ Claims 1 ~~to 3~~, characterized in that the channel system contains at least two parallel channel sections which are delimited independently of one another by fluidic connections.

5. (Amended) Apparatus according to ~~one of~~ Claims 1 ~~to 4~~, characterized in that tightly sealing micropumps serve as fluidic connections.

6. (Amended) Apparatus according to ~~one of~~ Claims 1 ~~to 4~~, characterized in that micromixers, valves and micropumps serve as fluidic connections.

Sample delivery apparatus

The invention relates to a sample delivery apparatus for planar miniaturized analytical systems.

In sectors such as food analysis, environmental analysis or industrial quality control, there is increasingly a need for analytical systems which enable exact and quantitative analysis of complex mixtures rapidly and without requiring a lot of apparatus. In addition to sensors for rapid tests which are based on specific chemical reactions and therefore are not universal methods, principally chromatographic and electrophoretic separation methods are useful. In contrast to most chromatographic and electrophoretic methods, isotachophoresis (ITP) offers the possibility of analysing large amounts of sample with high separation selectivity without previous workup. Electrophoretic separation methods such as ITP are also suitable for use in miniaturized analytical systems (MAS), so that the equipment requirements for analyses can be greatly reduced. An important advantage of the use of MAS is that these can be discarded after contamination. In order to achieve this advantage, the reproducibility of analyses in series and between different MASs of the same type must be ensured.

In addition to the analytical apparatus itself, one of the most important components of a miniaturized system is the sample delivery apparatus. Since methods such as, for example, ITP are highly variable with respect to sample properties and amounts, the sample delivery method determines the sample volume and type of sample that can be analysed.

In macroscopic analytical systems, mechanical delivery apparatuses for delivering a defined sample volume can be used similarly to the case of instruments for high-pressure liquid chromatography or instruments for

isotachophoresis. In Figure 4, by way of example, such a delivery apparatus of the prior art is described in more detail. The apparatuses generally consist of stopcock systems built up in a complex manner, some having integrated delivery loops. These apparatuses cannot be applied to miniaturized analytical systems, since rotatable stopcocks or other mechanical apparatuses, for example closable valves, cannot be correspondingly miniaturized.

Therefore, in the case of miniaturized analytical apparatuses based on capillary electrophoresis (CE) or ITP, apparatuses are used in which the sample is delivered electrokinetically utilizing the electroosmotic flow. This is termed electroosmotic sample delivery hereinafter. A diagrammatic set-up of such an apparatus of the prior art is shown in Figure 3. By means of crossed or crossed offset capillary structures, a sample volume is defined by a channel firstly being filled with sample. This can be achieved, for example, electroosmotically by applying a voltage. The electrodes in the filled channel are then switched to the same potential and a voltage is applied to the separation channel system situated perpendicularly thereto. In this manner, the sample volume which is situated at the point of intersection of the two channel systems is transported into the separation channel system. The sample volume thus generated is in the region of a few nanolitres or less.

Although it is possible in this manner to deliver a sample volume defined by the intersection of the channels, the volume elements in which mass transfer takes place with the side channels by diffusion are very large in relation to the sample volume defined by the intersection volume. Thus the sample volume which is actually introduced is subject to great variations. Since only very small sample volumes can be analysed, the concentration of certain analytes in the detection

region rapidly falls below the limit of detection or the sample volume taken cannot be considered as representative for the totality of the sample.

In addition, if the channel cross sectional area is sufficiently large, the sample can be delivered by hydrodynamic injection from a sample vessel. In this case, a part of the sample is transported by time-controlled application of a pressure difference between the external sample vessel and the start of the separation capillary. A disadvantage of this method is a high dependency of sample volume on sample properties (for example viscosity), but also on the achievable accuracy of pressure control. Even owing to this, delivering an exactly defined sample volume is not possible. In addition, there are also problems here due to diffusive or convective mass transfer at the interfaces between sample volume and adjacent volume units. In the case of commercial non-miniaturized systems, hydrodynamic injection is prior art, for miniaturized systems it offers no advantages over the above-described electrokinetic injection utilizing electroosmotic flow.

Direct electrophoretic injection from an external sample vessel (without utilizing electroosmotic flow), as also used in commercial instruments, is not suitable at all in principle for delivering defined volumes, since in this case no volumetric flow is generated in the sample solution, but only ions are transferred electrophoretically into the separation system.

A further fundamental disadvantage of all electro-osmotic methods results from the restricted choice of materials. Since sample transport is associated with the occurrence of an electroosmotic flow, a high charge density must be present on the material surface. In addition, even during delivery, electrophoretic

fractionation of the sample occurs, so that an inhomogeneous injection profile results.

Since by means of ITP relatively large sample volumes can be analysed without a problem, the analytical performance of the current miniaturized analytical systems are largely restricted by the unsatisfactory method for delivering large defined sample volumes.

The object of the present invention is therefore to develop a sample delivery apparatus which makes it possible to introduce defined variable sample volumes between 0.01 and 100 μl into a miniaturized analytical system.

It has been found that a delivery apparatus consisting of a channel system and fluidic connections for the liquid transport makes it possible to deliver large sample volumes in planar systems. By opening the system at the end of a channel section and simultaneously charging the channel section with the sample solution at the other end, a defined channel section is filled with the sample solution. The volume of the channel section and thus the sample volume delivered is defined by the geometry of the channel section, but is otherwise freely selectable.

The invention therefore relates to an apparatus for delivering defined sample volumes above 0.01 μl for miniaturized analytical systems, comprising chiefly at least one channel section at each end of which fluidic connections are present.

In a preferred embodiment of the apparatus, sample volumes between 0.05 and 30 μl can be delivered.

A preferred embodiment is further a delivery apparatus which contains at least two serial channel sections, each of which is delimited by fluidic connections. When

the two channel sections are directly adjacent, three fluidic connections are thus provided in total.

A preferred embodiment is also a delivery apparatus which contains a channel system having at least two parallel channel sections which are delimited independently of one another by fluidic connections.

A preferred embodiment is an apparatus which possesses, as fluidic connections, micromixers, valves and micropumps or tightly sealing micropumps.

Figure 1 shows an inventive delivery apparatus.

Figure 2 shows a possible procedure for charging a miniaturized analytical system by an inventive delivery apparatus.

Figure 3 shows a delivery apparatus for miniaturized analytical systems from the prior art.

Figure 4 shows a delivery apparatus for macroscopic analytical systems from the prior art.

In contrast to other delivery methods, in the case of the inventive apparatus, the channel system is open at two positions during sample delivery. One opening serves for introducing the liquid, that is to say for example the sample solution, the other opening enables the egress of the liquid or air previously present in the system. The principle of the inventive delivery apparatus is therefore displacement by the sample solution of a volume of liquid or gas situated in a defined channel section.

By a suitable choice of the inlet and outlet openings, only the liquid in the intermediate channel section is displaced, or the intermediate channel section is filled. The liquid in any adjacent side channels

present is not exchanged, since there are no open inlet or outlet openings in the side channels and thus the liquid in these regions is moved neither by pressure nor by suction. Losses or dilutions due to liquid streams on the contact surfaces to side channels are low in relation to the overall sample volume which is typically in the µl range. At a suitable constant metering rate, the sample can be delivered very reproducibly. This is a great advantage compared with methods in which very small sample volumes of a few nanolitres are delivered. An inventive delivery apparatus is also suitable in principle for delivery volumes of less than 50 nl. However, compromises are then necessary with respect to precision and accuracy.

The sample liquid can be transported via closely connected pumps, syringes, micromixers, electroosmosis or hydrostatic pressure, preferably via micropumps and valves.

These apparatuses can be mounted preferably externally, as close as possible to the chip.

The exiting liquid need not be additionally pumped off. It is sufficiently effectively displaced by the pressure of the injected replacement liquid.

This type of charging avoids the disadvantages of electroosmotic injection, that is to say charging is substantially independent of sample composition, pH and the material of the analytical system. By means of existing valves or tightly sealing pumps, any interfering liquid motion, for example due to hydrostatic pressure differences or electroosmosis, is prevented.

According to the invention, all valves, pumps or micropumps, tightly sealing micropumps, micromixers or other connections of the inventive apparatus which

serve for charging the channel system are termed fluidic connections.

The inventive delivery apparatus can be used for any type of planar miniaturized analytical system. These can be systems for analysis or else systems which additionally contain separation or derivatization units. Corresponding miniaturized systems are known to those skilled in the art.

Viscosity and ionic strength of the sample solution or of the solution to be displaced, that is to say for example a transport buffer, only have a small effect on metering or charging rate. It is possible to charge suspensions, emulsions, particle-containing and cell-containing liquids. Similarly, the choice of material for construction of the analytical apparatus is subject to no restriction, that is to say particularly the properties of the walls of the channel system of the inventive sample delivery apparatus. Pressure variations, pulses, start-up or shut-down effects during sample introduction also have no effect on metering accuracy.

The inventive apparatus has broad system-related limits with respect to delivery volume. The volume of sample liquid which can be injected is determined solely by the volume of the channel section which is situated between the openings. By varying the geometric dimensions of this section in the design of the channel system of the analytical apparatus, sample volumes matched to the analytical problem may be established in advance. Similarly, it is possible to implement differently-sized sections in parallel and/or in series, so that the volume of the section to be displaced by the sample solution can be varied. More preferably, therefore, an analytical system for using the inventive apparatus is provided with a plurality of channel sections of different dimensions which can be

used for sample delivery via respectively independent fluidic connections. By this means, sample volumes between 0.01 µl and 100 µl, preferably between 0.05 and 30 µl, at different steps, can be injected according to requirements. In this case, usually, coefficients of variation during delivery of sample volumes from 1 µl of about 5%, typically less than 2%, are achieved.

In this manner, quantitatively reproducible and readily handlable representative sample quantities of a liquid analyte can be introduced into any microstructured system. Particular preference is given to the use of the inventive apparatus for ITP, since this gives the possibility of enriching and separating very small amounts of analytes from large sample volumes.

Figure 1 shows, by way of example, a possible arrangement of the channel system of the inventive delivery apparatus. The channel system is subdivided into two channel sections 1A and 1B of different volumes. Adjacent thereto is the separation channel 1C. Via the fluidic connections 11, 12 and 13, either channel section 1A (when connections 11 and 12 are open) or channel section 1B (during charging via connections 12 and 13) or the two channel sections together (during charging via connections 11 and 13) can be filled with the sample solution. After charging the delivery sections, by applying a voltage the sample is fractionated in section 1C. If only section 1A was filled with the sample, section 1B can also be used as separation path, so that the separation path can be extended if required.

Figure 2 shows a possible procedure for charging a miniaturized analytical system. The figure shows a channel system consisting of three reservoirs R1 to R3, the channel sections K1 to K4, the fluidic connections F1 to F6 and a branching point Vz. The system shown in the figure has a channel section K1 for sample

delivery. The separation can be performed along channel section K2 and K3, or K2 and K4. To carry out an isotachophoretic separation, the system must be charged with a sample and appropriate buffers. In this case, the sample volume must be in contact with one buffer (leading buffer) at one end in the direction of the separation path and with another buffer (terminating buffer) at the other end. As a result of the branching Vz of the channel system, there is the possibility of charging different leading buffers via reservoirs R2 and R3. Components which have been fractionated from the sample can be discharged via the fluidic connection F3.

In order to achieve the desired arrangement of sample and buffers in the channel system, firstly, as shown diagrammatically under A in the figure, the fluidic connections F2 (outlet), F4, F5 and F6 (inlets) are open, and the channel system is filled via the three reservoirs with the two leading buffers (via R2 and R3, shown hatched and dotted, respectively) and the terminating buffer (via R1, shown with vertical stripes). Excess buffer can exit via the fluidic connection F2. In this manner, channel section K1 fills with terminating buffer, section K3 with leading buffer (LE2) via R2, section K4 with leading buffer (LE1) via R3 and channel section K2 contains a mixture of the two leading buffers. The fluidic connections F1 and F3 remain closed during this step.

Channel section K2 can be filled with leading buffers optionally via R2 or R3. K2 is the first section of the separation path.

Part B of the figure shows how the sample is introduced into channel section K1 and the channel section K2 is filled with a leading buffer via R3. The fluidic connections F5 and F6 are closed and no further trailing buffer is pumped via R1 and no further leading

buffer (LE2) is pumped via R2. Fluidic connection F4 is open and channel section K2 is filled with leading buffer (LE1) via R3. At the same time, fluidic connection F1 is open and the sample is fed via F1 (shown as wavy lines). Excess sample and excess leading buffer (LE1) can exit via the open fluidic connection F2. By the leading buffer (LE1) and the sample volume being pumped simultaneously against one another, a particularly precise filling of channel sections K1 and K2 is achieved. In this manner, it is possible to perform exact charging even using pumps which have a slight pulsation.

After completion of the filling operation, the fluidic connections are closed. This thus produces a closed system without hydrodynamic flow in which the separation can be carried out reproducibly. The sample can be separated completely or in fractions via the channel sections K2 and K3 or via the channel sections K2 and K4. As soon as the sample or a chosen fraction has migrated through the channel section K2 and has arrived at the branch Vz, a decision can be made as to whether separation is to be carried out further in the direction of K4 or K3. This is achieved by switching over the anode potential from F4 to F6 for a long period or temporarily.

The table below shows again in outline the switching of the fluidic connections during the individual sample delivery steps:

Filling process	Fluidic connections					
	F1	F2	F3	F4	F5	F6
Filling process A	closed	open, "over-flow"	closed	open (LE1 in)	open (TE in)	open (LE2 in)
Filling process B	open (sample in	open, "over-flow"	closed	open (LE1 in)	closed	closed

After completion of the filling operation, the fluidic connections (F1-F6) are closed.

Below, by way of example, some switching processes are listed for various analytical processes on an analytical unit corresponding to Figure 2:
(The voltage is applied in each case downstream of the fluidic connections)

1.) Simple separation (separation channels K2 and K4)
Anode: F4 Cathode: F5

2.) 2-stage separation (discharge into internal channel K3)
a.) Separation in K2 Anode: F4 Cathode: F5
(Switchover when sample component is just upstream of Vz)
b.) Separation in K3 Anode: F6 Cathode: F5

3.) 2-stage separation (discharge and transfer to external channel)
a.) Separation in K2 Anode: F4 Cathode: F5
(Switchover when sample component is just upstream of Vz)
b.) Transfer to the exterior via F3
Anode: F3 Cathode: F5

Figure 3 shows a possible method for electrokinetic sample delivery in miniaturized analytical systems from the prior art. Figures A, B, C and D show the individual steps of sample delivery. Figure A shows diagrammatically a crossed channel structure. At the ends of the channels are situated the electrodes E1 to E4. First, as shown in Figure B, a channel is filled with sample by applying a voltage between electrode E1 (0 V) and E2 (+500 V). Then, as shown in Figure C, the electrodes in the filled channel are switched to the same potential (for example E1 and E2 both at +400 V) and a voltage is applied to the separation channel system situated perpendicularly thereto (E3 = 0 V and E4 = +2.5 kV). In this manner, the sample volume which is situated at the intersection of the two channel systems is transported into the separation channel system (Figure D). The sample volume thus produced is in the range of some nanolitres or less.

Figure 4 shows a possible method for sample delivery in macroscopic analytical systems, for example the isotachophoresis instrument ItaChrom® EA 101 from I+M, Analytische Meß- und Regeltechnik, Germany. Figures A1/A2, B1/B2 and C1/C2 show the different sample delivery steps, with Figures A1, B1 and C1 showing a side view of the delivery apparatus, and Figures A2, B2 and C2 showing a view from above. This mechanical sample delivery apparatus consists of a stopcock K which is surrounded by a casing U. Both the casing U and the stopcock K are multiply pierced by channels. The stopcock K can be rotated in the casing U in such a manner that in each case defined channels in the stopcock and casing are connected and liquids thus pass from storage vessels via the apparatus shown in a defined manner into the connected isotachophoresis instrument. Storage vessels and the ITP instrument are not shown in the figure, but only indicated by arrows. In Figures A1/A2, the stopcock is rotated so that there is a connection between channel pieces 3, 4 and 5, and

between 2 and 6. By this means, channel piece 5 in the interior of the stopcock is filled with sample solution from a storage vessel which is connected to channel 3. In addition, via a storage vessel on channel 2, the channel system of the isotachophoresis instrument is filled with one of the two separation buffers (buffer 1) necessary for ITP.

In a second step (Figure B1/B2), the stopcock K is rotated so that the channel connections existing in Figure A1/A2 are broken. Instead, a connection is made between channel pieces 1 and 7. In this manner, the channel system situated downstream of the delivery apparatus is filled with a second buffer (buffer 2). In Figure C1/C2, finally stopcock K is rotated again so that a connection is formed between channel pieces 1, 5 and 2. Channel 2 is filled with buffer 1, channel 5 with the sample solution and channel 1 with buffer 2. In this manner, a sample solution volume defined by the dimensions of channel 5 is embedded between the two buffers necessary for ITP. By applying a voltage, the separation can then be begun.

Even without further explanations, it is assumed that a person skilled in the art can utilize the above description to the broadest extent. The preferred embodiments and examples are therefore to be understood only as descriptive disclosure which is in no way limiting in any sense.

Complete disclosure of all applications, patents and publications listed above and below and of the corresponding application DE 199 27 534, submitted on 16.06.1999, is incorporated by reference into this application.

Claims

1. Apparatus for delivering defined sample volumes above 0.01 µl for miniaturized analytical systems, comprising at least one channel section at each end of which at least one fluidic connection is present.

2. Apparatus according to Claim 1, characterized in that the sample volume is between 0.05 and 30 µl.

3. Apparatus according to Claim 1 or 2, characterized in that the channel system contains at least two serial channel sections, each of which is delimited by fluidic connections.

4. Apparatus according to one of Claims 1 to 3, characterized in that the channel system contains at least two parallel channel sections which are delimited independently of one another by fluidic connections.

5. Apparatus according to one of Claims 1 to 4, characterized in that tightly sealing micropumps serve as fluidic connections.

6. Apparatus according to one of Claims 1 to 4, characterized in that micromixers, valves and micropumps serve as fluidic connections.

Fig. 1

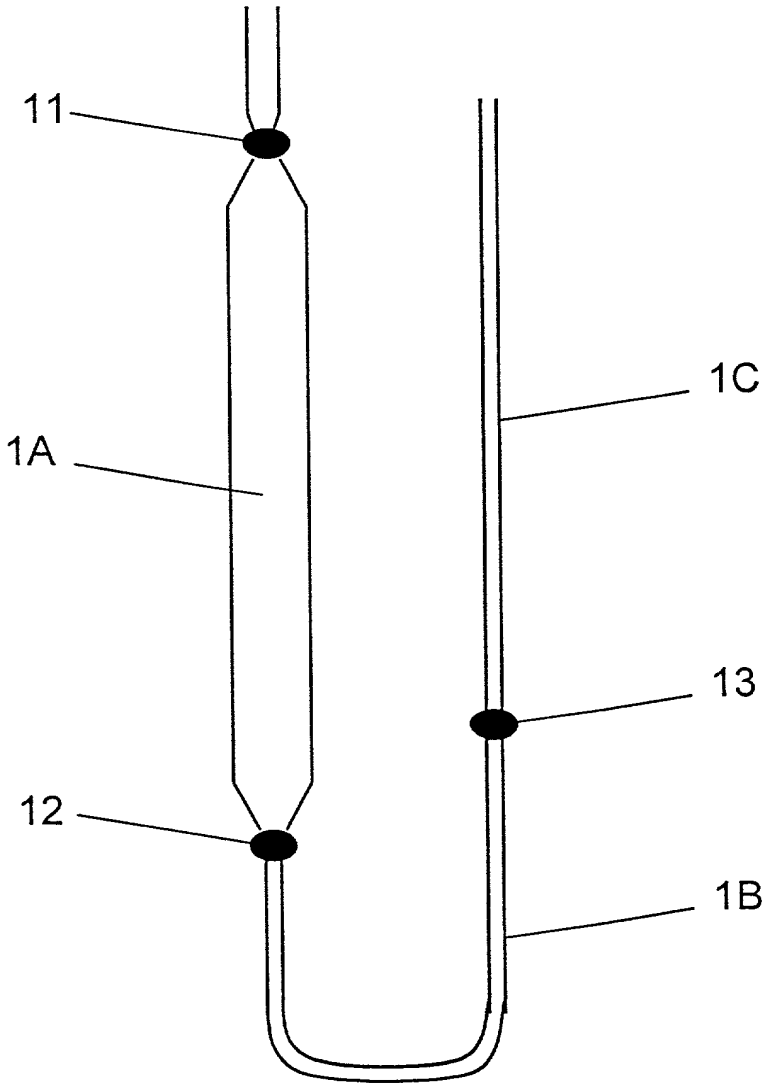
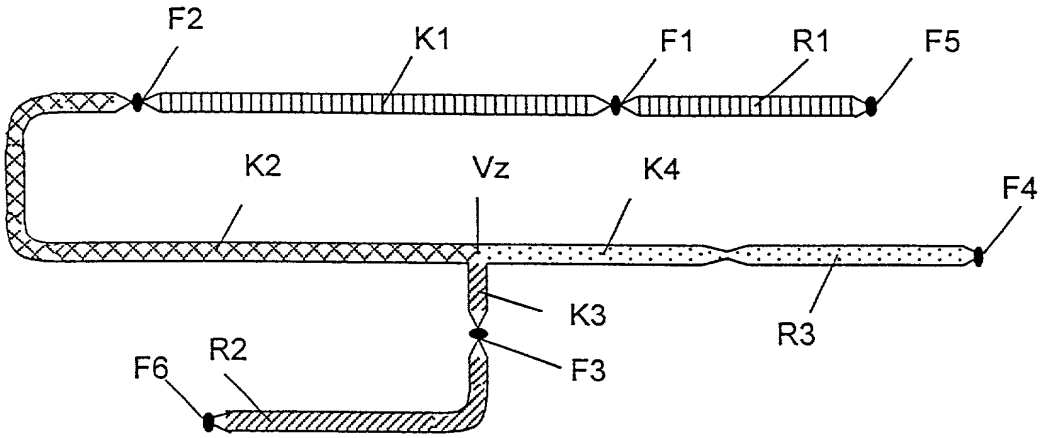
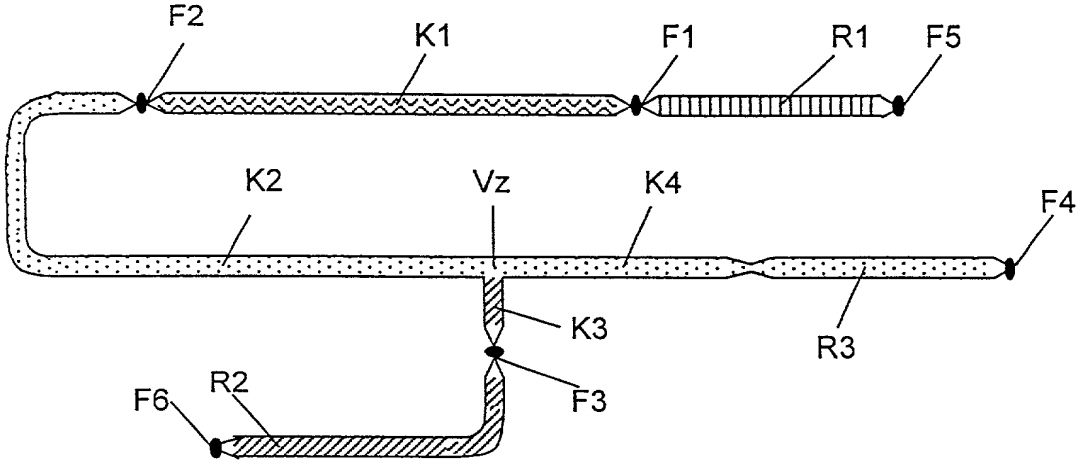


Fig. 2

A


F2
K1
F1
R1
F5
K2
Vz
K4
F4
K3
R3
F6
R2
F3

B


F2
K1
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R1
F5
K2
Vz
K4
F4
K3
R3
F6
R2
F3

Fig. 3

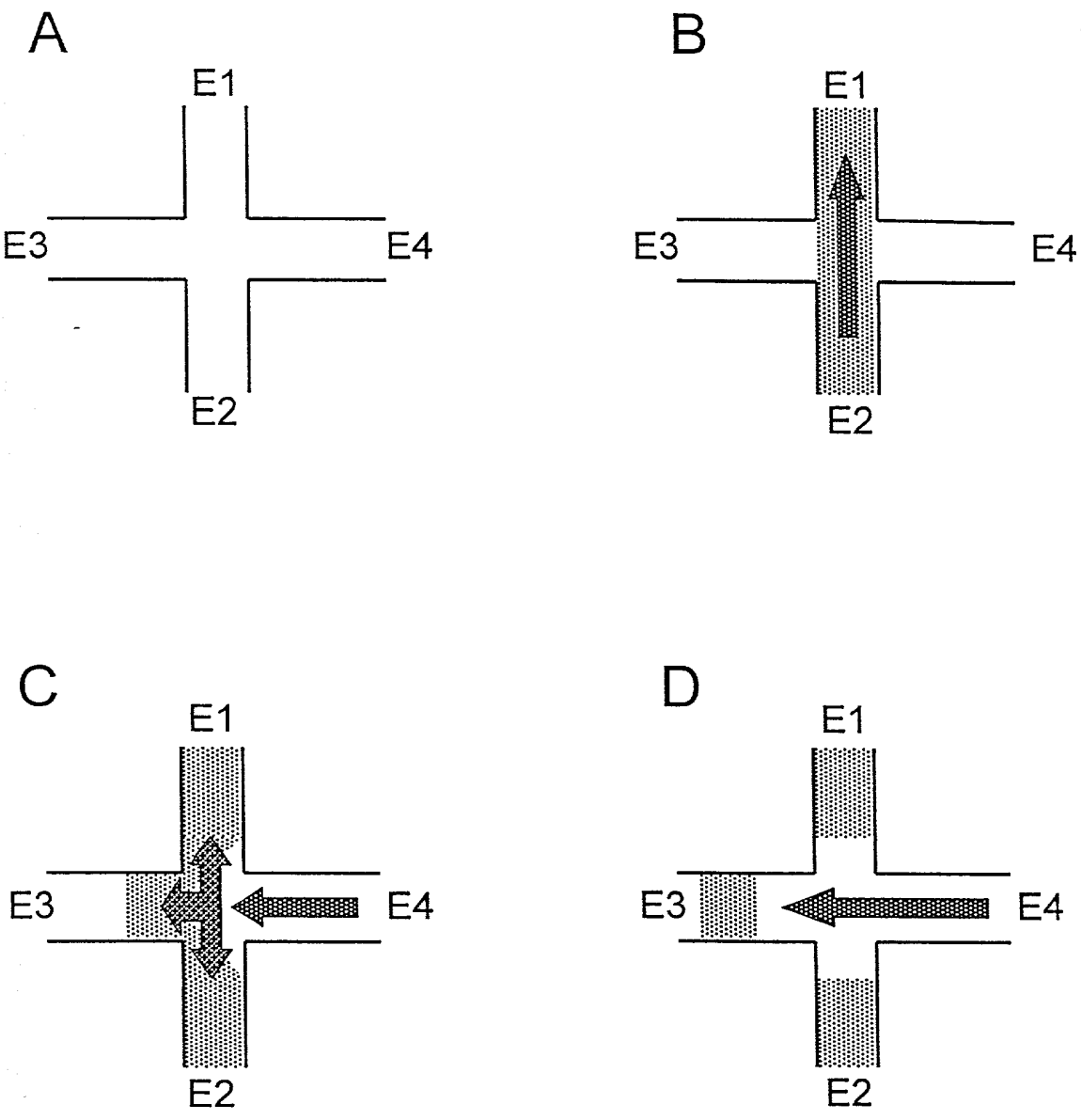
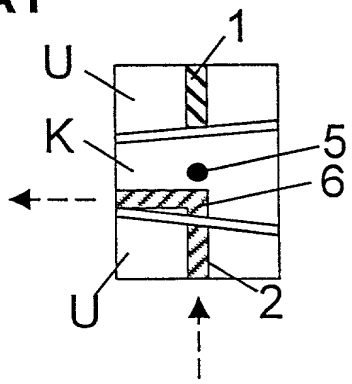
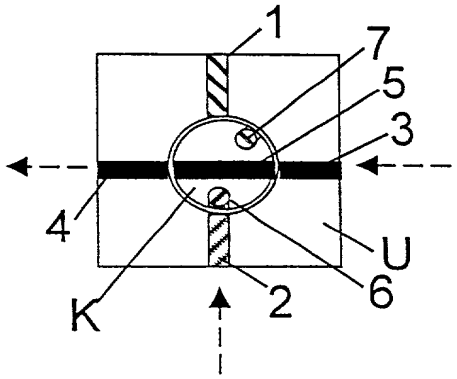


Fig. 4

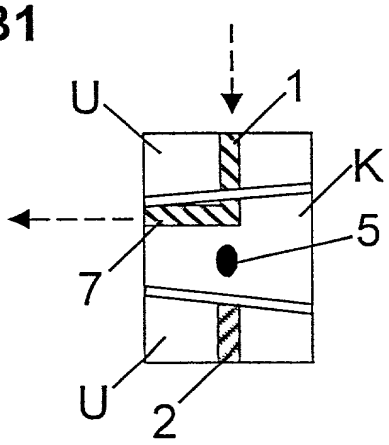
A1



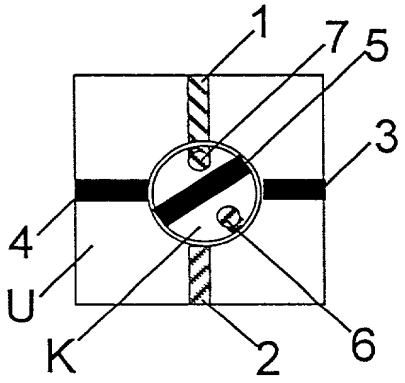
A2



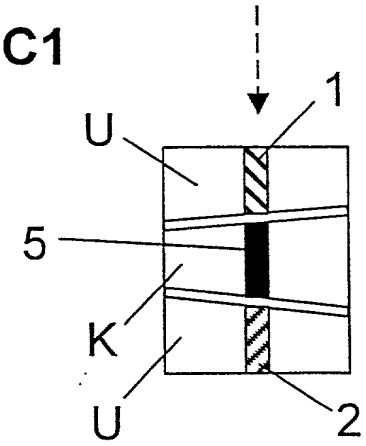
B1



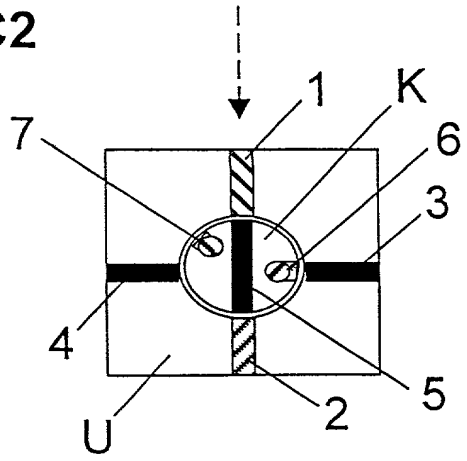
B2



C1



C2



COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to PCT International Applications)

ATTORNEY'S DOCKET NUMBER

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought of the invention entitled:

Device for Introducing Samples

the specification of which (check only one item below):

☐ is attached hereto.

☐ was filed as United States application

Serial No. _____

on _____

and was amended

on _____ (if applicable).

☒ was filed as PCT international application

Number PCT/EP00/05204

on 6. June 2000

and was amended under PCT Article 19

on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim priority benefits under Title 35, United States Code, §119 of the following United States Provisional Application and of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR U.S. PROVISIONAL AND FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
Germany	199 27 534.3	16. June 1999	☒ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO

Combined Declaration For Patent Application and Power of Attorney (Continued)
(Includes Reference to PCT International Applications)

ATTORNEY'S DOCKET NUMBER

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

PCT APPLICATION NO.	PCT FILING DATE	U.S. SERIAL NUMBERS ASSIGNED (*if any*)			

POWER OF ATTORNEY: As a named inventor, I hereby appoint I. William Millen (19,544); John L. White (17,746); Anthony J. Zelano (27,969); Alan E.J. Branigan (20,565); John R. Moses (24,983); Harry B. Shubin (32,004); Brion P. Heaney (32,542); Richard J. Traverso (30,595); John A. Sopp (33,103); Richard M. Lebovitz (37,067); John H. Thomas (33,460); Catherine M. Joyce (40,668); James T. Moore (35,619), James E. Ruland (37,432), Nancy Axelrod (44,014) and Jennifer J. Branigan (40,921) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

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Combined Declaration for Patent Application and Power of Attorney (Continued)
(Includes Reference to PCT International Applications)

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	RESIDENCE & CITIZENSHIP	CITY:	STATE OR FOREIGN COUNTRY:	COUNTRY OF CITIZENSHIP:
	POST OFFICE ADDRESS	STREET:	CITY:	STATE & ZIP CODE/COUNTRY:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	DATE: 24.10.2001	SIGNATURE OF INVENTOR 207	DATE: 24.10.2001
SIGNATURE OF INVENTOR 202	DATE: 24.10.2001	SIGNATURE OF INVENTOR 208	DATE: 24.10.2001
SIGNATURE OF INVENTOR 203	DATE: 24.10.2001	SIGNATURE OF INVENTOR 209	DATE: 24.10.2001
SIGNATURE OF INVENTOR 204	DATE: 24.10.2001	SIGNATURE OF INVENTOR 210	DATE:
SIGNATURE OF INVENTOR 205	DATE: 24.10.2001	SIGNATURE OF INVENTOR 211	DATE:
SIGNATURE OF INVENTOR 206	DATE: 24.10.2001	SIGNATURE OF INVENTOR 212	DATE: